

AMENDMENTS TO THE CLAIMS

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Claim 1 (currently amended): A substantially pure α -conotoxin peptide having the generic formula I: Xaa₁-Xaa₂-Xaa₃-Xaa₄-Xaa₅-Cys-Cys-Xaa₆-Xaa₇-Xaa₈-Xaa₉-Cys-Xaa₁₀-Xaa₁₁-Xaa₁₂-Cys-Xaa₁₃ (SEQ ID NO1:), wherein Xaa₁ is des-Xaa₁, Ile, Leu or Val; Xaa₂ is des-Xaa₂, Ala or Gly; Xaa₃ is des-Xaa₃, Gly, Trp (D or L), neo-Trp, halo-Trp or any unnatural aromatic amino acid; Xaa₄ is des-Xaa₄, Asp, Phe, Gly, Ala, Glu, γ -carboxy-Glu (Gla) or any unnatural aromatic amino acid; Xaa₅ is Glu, Gla, Asp, Ala, Thr, Ser, Gly, Ile, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa₆ is Ser, Thr, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa₇ is Asp, Glu, Gla, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa₈ is Ser, Thr, Asn, Ala, Gly, Arg, Lys, ornithine, homoarginine, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys, any unnatural basic amino acid, His, halo-His, Pro or hydroxy-Pro; Xaa₉ is Thr, Ser, Ala, Asp, Asn, Pro, hydroxy-Pro, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa₁₀ is Gly, Ser, Thr, ~~Ala~~, Asn, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa₁₁ is Gln, Leu, His, halo-His, Trp (D or L), halo-Trp, neo-Trp, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys, any unnatural basic amino acid or any unnatural aromatic amino acid; Xaa₁₂ is Asn, His, halo-His, Ile, Leu, Val, Gln, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa₁₃ is des-Xaa₁₃, Val, Ile, Leu, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; and the C-terminus contains a free carboxyl group or an amide group.

Claim 2 (currently amended): A substantially pure α -conotoxin peptide of generic formula I selected from the group consisting of:

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conclude*

~~Asp-Xaa₁-Cys-Cys-Ser-Asp-Ser-Arg-Cys-Gly-Xaa₂-Asn-Cys-Leu (SEQ ID NO:4);~~
~~Ala-Cys-Cys-Ser-Asp-Arg-Arg-Cys-Arg-Xaa₃-Arg-Cys (SEQ ID NO:5);~~
~~Phe-Thr-Cys-Cys-Arg-Arg-Gly-Thr-Cys-Ser-Gln-His-Cys (SEQ ID NO:6);~~
~~Asp-Xaa₄-Cys-Cys-Arg-Arg-His-Ala-Cys-Thr-Leu-Ile-Cys (SEQ ID NO:7);~~
~~Asp-Xaa₄-Cys-Cys-Arg-Xaa₃-Xaa₃-Cys-Thr-Leu-Ile-Cys (SEQ ID NO:8);~~
~~Gly-Cys-Cys-Ser-Asp-Xaa₃-Arg-Cys-Arg-Xaa₄-Arg-Cys-Arg (SEQ ID NO:9);~~
~~Gly-Gly-Cys-Cys-Ser-Asp-Xaa₃-Arg-Cys-Ala-Xaa₃-Arg-Cys (SEQ ID NO:10);~~
~~Ile-Ala-Xaa₃-Asp-Ile-Cys-Cys-Ser-Xaa₁-Xaa₃-Asp-Cys-Asn-His-Xaa₂-Cys-Val (SEQ ID NO:11); and a derivative thereof.~~

Gly-Cys-Cys-Ser-Asp-Xaa₃-Arg-Cys-Xaa₂-His-Gln-Cys (SEQ ID NO:12);
wherein Xaa₁ is Glu or γ -carboxy-Glu (Gla); Xaa₂ is Lys, N-methyl-Lys, N,N-dimethyl-Lys or N,N,N-trimethyl-Lys; Xaa₃ is Trp (D or L), halo-Trp or neo-Trp; Xaa₄ is Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or nitro-Tyr; and Xaa₅ is Pro or hydroxy-Pro; and the C-terminus contains a carboxyl or amide group, or derivatives thereof.

~~Claims 3-7 (canceled)~~

Claim 8 (original): The substantially pure α -conotoxin peptide of claim 1, which is modified to contain an O-glycan, an S-glycan or an N-glycan.

Claim 9 (original): The substantially pure α -conotoxin peptide of claim 2 which is modified to contain an O-glycan, an S-glycan or an N-glycan.

~~Claims 10-38 (canceled)~~

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Claim 39 (currently amended): A substantially pure α -conotoxin protein precursor comprising the ~~an~~ amino acid sequence Phe Asp Gly Arg Asn Ala Pro Ala Asp Asp Lys Ala Ser Asp Leu Ile Ala Gln Ile Val Arg Arg Ala Cys Cys Ser Asp Arg Arg Cys Arg Trp Arg Cys Gly (SEQ ID NO:236) ~~selected from the group of amino acid sequences set forth in Tables 1-134.~~

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Claim 40 (new): The substantially pure α -conotoxin peptide of claim 2, wherein the derivative is the amino acid sequence of SEQ ID NO:5, which comprises at least one of the following substitutions: an Arg residue is substituted by Lys, ornithine, homoarginine, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; a Ser residue is substituted with Thr; a Trp residue is substituted with any unnatural aromatic amino acid; a Cys residue is substituted with Cys (D) or homocysteine (D or L); an acidic amino acid residue is substituted with any synthetic acidic bioisoteric amino acid surrogate.

Claim 41 (new): The substantially pure α -conotoxin peptide of claim 40, wherein the synthetic acidic bioisoteric amino acid surrogate is selected from the group consisting of a tetrazolyl derivative of Gly and a tetrazolyl derivative of Ala.